I U C L I D

RECEIVED
OPPT CBIC

2003 SEP 12 PM 12:03

Data Set

Existing Chemical	:	ID: 101-84-8
CAS No.	:	101-84-8
EINECS Name	:	diphenyl ether
EINECS No.	:	202-981-2
TSCA Name	:	Benzene, 1,1'-oxybis-
Molecular Formula	:	C12H10O

Producer Related Part

Company	:	Solutia Inc./Dow Chemcial Co.
Creation date	:	25.09.2000 Updated 18.07.2003

Substance Related Part

Company	:	Solutia Inc./ Dow Chemical Co.
Creation date	:	25.09.2000 Updated 18.07.2003

Memo	:	
Printing date	:	18.7.2003
Revision date	:	
Date of last Update	:	18.7.2003
Number of Pages	:	1
Chapter (profile)	:	Chapter: 1, 2, 3, 4, 5, 7
Reliability (profile)	:	Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	:	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 OECD AND COMPANY INFORMATION

1.0.2 LOCATION OF PRODUCTION SITE

1.0.3 IDENTITY OF RECIPIENTS

1.1 GENERAL SUBSTANCE INFORMATION

1.1.0 DETAILS ON TEMPLATE

1.1.1 SPECTRA

1.2 SYNONYMS

1.3 IMPURITIES

1.4 ADDITIVES

1.5 QUANTITY

1.6.1 LABELLING

1.6.2 CLASSIFICATION

1.7 USE PATTERN

1.7.1 TECHNOLOGY PRODUCTION/USE

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUES

1.9 SOURCE OF EXPOSURE

1.10.1 RECOMMENDATIONS/PRECAUTIONARY MEASURES

1.10.2 EMERGENCY MEASURES

1.11 PACKAGING

1.12 POSSIB. OF RENDERING SUBST. HARMLESS

1.13 STATEMENTS CONCERNING WASTE

1.14.1 WATER POLLUTION

1.14.2 MAJOR ACCIDENT HAZARDS

1.14.3 AIR POLLUTION

1.15 ADDITIONAL REMARKS

1.16 LAST LITERATURE SEARCH

1.17 REVIEWS

1.18 LISTINGS E.G. CHEMICAL INVENTORIES

2.1 MELTING POINT

Value	:	28 ° C
Sublimation	:	
Method	:	other
Year	:	1983
GLP	:	no data
Test substance	:	other TS
Method	:	not referenced
Test substance	:	Diphenyl oxide
Reliability	:	(2) valid with restrictions Citation in reputable, universally accepted reference guide.
Flag	:	Critical study for SIDS endpoint

25.11.2002 (16)

2.2 BOILING POINT

Value	:	257 - 259 ° C at
Decomposition	:	
Method	:	other
Year	:	1983
GLP	:	no data
Test substance	:	other TS
Method	:	not referenced
Test substance	:	Diphenyl oxide
Reliability	:	(2) valid with restrictions Citation in reputable, universally accepted reference guide.
Flag	:	Critical study for SIDS endpoint

25.11.2002 (16)

2.3 DENSITY

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value	:	.02 mm Hg at 25° C ; 0.12 mm Hg at 30 deg. C.
Decomposition	:	
Method		other (measured)
Year	:	1983
GLP	:	no data
Test substance	:	other TS
Method	:	not referenced
Result	:	
Test substance	:	Diphenyl oxide
Reliability	:	(2) valid with restrictions Citation in reputable, universally accepted reference guide.
Flag	:	Critical study for SIDS endpoint

25.11.2002 (16)

2.5 PARTITION COEFFICIENT

Log pow	:	4.2 at 20° C
Method		OECD Guide-line 107 "Partition Coefficient (n-octanol/water), Flask-shaking Method"
Year	:	1980
GLP	:	no data
Test substance	:	other TS
Method	:	Additional estimated value derived for comparison using KOWWIN (1997), Syracuse Research Corp., Syracuse, NY
Test substance	:	Diphenyl oxide
Reliability	:	(1) valid without restriction
Remark		Measured value obtained from study design similar to OECD 107. This value is consistent with estimated log Pow value of 4.1 using Octanol-Water Partition Coefficient Program KOWWIN from Syracuse Research Corporation, 1997. Log Kow values are often used to predict the potential for a compound to bioconcentrate in aquatic organisms. The measured bioconcentration factor for diphenyl oxide in rainbow trout has been reported to be 196, indicating significant metabolic clearance of the compound from the fish [Neely, W. B., Branson, D. R., and Blau, G. E. 1974. Environ. Sci. Technol., 8:1113-1115; these data are also found in Dow report WCL-73015: DR Branson, NH Litchfield, and HC Alexander. 1973. Bioconcentration of diphenyl oxide in trout. DR-0000-7307-099-WCL73015].
Flag	:	Critical study for SIDS endpoint

25.11.2002 (2)

2.6.1 WATER SOLUBILITY

Value	:	21 ppm at 25 ° C
Qualitative	:	
Pka	:	
PH	:	
Method	:	other
Year	:	1980
GLP	:	no data
Test substance	:	other TS
Method	:	not referenced
Test substance	:	Diphenyl oxide
Reliability	:	(2) valid with restrictions Citation is from reputable, universally accepted reference guide and also consistent with estimated value of 16 ppm derived from structure-activity relationships from the Water Solubility Log Kow Program from Syracuse Research Corp., 1997.
Flag	:	Critical study for SIDS endpoint

25.11.2002 (16)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

2.8 AUTO FLAMMABILITY

2.9 FLAMMABILITY

2.10 EXPLOSIVE PROPERTIES

2.11 OXIDIZING PROPERTIES

2.12 ADDITIONAL REMARKS

3.1.1 PHOTODEGRADATION

Indirect photolysis

Sensitizer	:	OH
Conc. of sens.	:	1600000 molecule/cm3
Rate constant	:	.0000000000098 cm3/(molecule*sec)
Degradation	:	50 % after 1.1 day
Deg. Product	:	
Method	:	other (calculated)
Year	:	1997
GLP	:	
Test substance	:	other TS
Method	:	Estimation using the AOP model (Atmospheric Oxidation Program), version 1.9. Syracuse Research Corporation, 1997.
Reliability	:	(2) valid with restrictions Computer estimation model recommended for use by US EPA.
Flag	:	Critical study for SIDS endpoint

25.11.2002 (1)

3.1.2 STABILITY IN WATER

Value	:	Diphenyl oxide not susceptible to hydrolysis under environmental conditions
Remark	:	Compound does not contain hydrolyzable functional groups. Lyman, W. J., Reehl, W. F., Rosenblatt, D. H. 1982. Handbook of Chemical Property Estimation Methods. Environmental Behavior of Organic Compounds. McGraw-Hill Book Company, New York, NY. Estimation program cannot predict hydrolysis rate due to lack of hydrolyzable groups [Syracuse Research Corporation; Aqueous Hydrolysis Rate Program HYDROWIN; 1996].
Method		
Year	:	
GLP	:	
Test substance	:	
Method	:	
Result	:	
Test substance	:	Diphenyl oxide
Reliability	:	(2) valid with restrictions Citation in reputable, universally accepted reference guide.
Flag	:	Critical study for SIDS endpoint

25.11.2002 (16)

3.1.3 STABILITY IN SOIL

3.2 MONITORING DATA

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type	:	Fugacity model level I (version 2.11)
Media	:	other

Method : Input parameters
Molecular mass (g/mol) = 170.2
Temperature (°C) = 25
Log Kow = 4.2
Water Solubility (g/m^3) = 21
Vapor Pressure (Pa) = 2.67
Henry's Law Constant (Pa.m^3/mol) = 21.6
Melting Point (°C) = 28

Results
Distribution of DPO:

22.1% to Air	0.004% to Biota (Fish)
5.1% to Water	0.05% to Suspended Sediment in Water
1.6% to Sediment	<0.001% to Aerosols
71.2% to Soil	

Year : 2002
Method : Estimation based on fugacity calculations
Reliability : (2) valid with restrictions
Flag : Supplemental study for SIDS endpoint
26.11.2002

Type : fugacity model level III
Media : other
Air (level I) : 4.47
Water (level I) : 28.9
Soil (level I) : 63.7
Biota (level II / III) :
Soil (level II / III) : 2.87
Method : other
Year : 2002
Method : Calculated according to MacKay, using EPIWIN 3.05, EQC Level III. Assumed emissions (1000 kg/hr) to air, water and soil compartments using measured values as available from this reference document. Last soil entry included data estimate for sediments.

Results

```
Level III Fugacity Model (Full-Output):
=======================================
  Chem Name    : Diphenyl oxide
  Molecular Wt: 170.21
  Henry's LC   : 0.000279 atm-m3/mole (Henry database)
  Vapor Press : 0.02 mm Hg  (user-entered)
  Liquid VP    : 0.0214 mm Hg  (super-cooled)
  Melting Pt   : 28 deg C (user-entered)
  Log Kow      : 4.2  (user-entered)
  Soil Koc     : 6.5e+003  (calc by model)

           Concentration   Half-Life    Emissions
             (percent)        (hr)       (kg/hr)
   Air       4.47            26.7         1000
   Water     28.9            360          1000
   Soil      63.7            360          1000
   Sediment  2.87            1.44e+003    0


              Fugacity    Reaction    Advection   Reaction
Advection
               (atm)       (kg/hr)      (kg/hr)    (percent)
(percent)
   Air       5.21e-011    941         363         31.4
12.1
   Water     1.91e-009    453         235         15.1
7.84
   Soil      3.02e-010    996         0           33.2
```

```
0
   Sediment  6.08e-010    11.2        0.466       0.373
0.0155

   Persistence Time: 271 hr
   Reaction Time:    338 hr
   Advection Time:   1.36e+003 hr
   Percent Reacted:  80
   Percent Advected: 20

   Half-Lives (hr), (based upon Biowin (Ultimate) and Aopwin):
      Air:      26.74
      Water:    360
      Soil:     360
      Sediment: 1440
        Biowin estimate: 2.809  (weeks       )

   Advection Times (hr):
      Air:      100
      Water:    1000
      Sediment: 5e+004
```

Reliability : (2) valid with restrictions
Estimated values based on model recommended by US EPA.
Flag : Critical study for SIDS endpoint
26.11.2002

3.3.2 DISTRIBUTION

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type : aerobic
Inoculum : activated sludge, domestic
Concentration : 3mg/l related to Test substance
related to
Contact time : 20 weeks
Degradation : 51 - 94 % after 7 day
Result : Study showed that DPO was susceptible to primary biodegradation)
Deg. Product :
Method : other
Year : 1983
GLP : no
Test substance : other TS
Method : Biodegradation screening was carried out using a semi-continuous activated sludge (SCAS) procedure for primary biodegradation. Study design was patterned after the standard method as found in JAOCS 42:986 (1965) and JAOCS 46:432 (1969). Mixed liquor from a local domestic waste treatment plant was charged to a magnetically-stirred vessel of 1.5 L capacity. Means for aeration and liquid sampling were provided. The SCAS unit was operated on a 24-h cycle. At the beginning of each cycle, DPO at a rate of 3 (second through sixth week), 10 (seventh through fourteenth week) or 50 (fifteenth through twentieth test week) mg/L and sewage were added to the mixed liquor. Aeration was maintained until the end of the cycle, at which time the sludge was settled and supernatant drained. The cycle was then re-initiated by the addition of tap water, sewage and test material. Primary biodegradation was determined during

		one cycle each week by analyzing 50 ml mixed liquor samples drawn at the end of the cycle. The test was terminated after 20 weeks. Volatility loss was monitored for one complete cycle. A mean loss of 28% due to volatility was observed versus an overall loss of >94% at the low dose tested and 54% at the high dose during the same period. Thus, biotransformation was still the predominant proces for biodegradability in this study, particularly at the lowest feed level. DPO was extracted from the mixed liquor sample using hexane, and analyzed by GC fit with an FID detector. Mean recovery of earlier spiking samples was 93%.
Result	:	Nearly complete disappearance (>94%) was noted at the lowest feed level tested. At the intermediate feed level, the disappearance rate dropped to 54 % and to 51% at the highest feed level in a concentration dependent manner. Mean volatility losses for DPO were 28%.
Test substance	:	unspecified but likely commercial grade with purity > 99%
Reliability	:	(2) valid with restrictions Used well established methodology for determination of this endpoint. Results were consistent with other biodegradation studies cited in the EUB IUCLID for DPO (2000).
Flag	:	Critical study for SIDS endpoint

25.11.2002 (11)

Type	:	Aerobic
Inoculum	:	Secondary effluent from domestic wastewater treatment plant
Concentration	:	4.75 mg/l of test substance
Contact time	:	20 days
Degradation	:	Biodegradation reported as percent of theoretical oxygen demand: 5 days – 64% 10 days – 76% 20 days – 76%
Result	:	Study showed substantial biodegradation of test substance
Deg. Product	:	Not determined
Method	:	Biochemical Oxygen Demand (BOD) test described in Standard Methods for the Examination of Water and Wastewater, 14th Edition. 1975.
Year	:	1976
GLP	:	no
Test substance	:	Diphenyl oxide, industrial grade, unspecified but purity likely to be > 99%
Method	:	Dilution water was prepared with inorganic nutrients and buffer and inoculated with secondary effluent from the Midland, Michigan Municipal Wastewater Treatment Plant. Test substance was added at a nominal concentration of 4.75 mg/L and incubated for 20 days at 20 °C in separate glass bottles. Oxygen measurements were made at 5, 10, and 20 days. Biodegradation was measured based on oxygen consumption and reported as a percentage of the theoretical oyxgen demand for the test substance. Results were corrected for background oxygen consumption measured in control solutions (inoculated dilution water without test substance added).
Reliability	:	(2) valid with restrictions Used well established methodology for determination of this endpoint. Results were consistent with other biodegradation studies cited in the EUB IUCLID for DPO (2000).
Flag	:	Critical study for SIDS endpoint

11.7.2003 (4)

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

Type	:	static
Species	:	*Oncorhynchus mykiss* (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	ug/l (micrograms/L or ppb)
Analytical monitoring	:	Yes, fish tissue and aquarium water were both analyzed for ^{14}C activity
Exposure Concentrations	:	Forty fish exposed to 2.8 ug/L, in triplicate Forty fish exposed to 0.4 ug/L, in triplicate Forty control fish, in triplicate
Method	:	other
Year	:	1973
GLP	:	No
Test substance	:	^{14}C-radiolabeled diphenyl oxide (DPO); 50 uCi/mg specific activity; >99% pure
Test organism		10-13 cm in total length and 8-10 grams in weight
Method	:	Rainbow trout (*Oncorhynchus mykiss*) were placed in a flow-through exposure to ^{14}C-radiolabeled DPO for 96 hours and then transferred to fresh water for a 96 hour clearance period. Fish were exposed separately to either a mean, measured concentration of 0.4 ug/L or 2.8 ug/L. The flow-through system provided a turnover rate of approximately 1 L/g-fish/day and triplicate 12-L aquaria were used, with a total of forty fish for each exposure and control. To experimentally confirm the steady-state concentrations in each short-term, 96-hour exposure, longer term, 42-day exposures (plus a control) were also conducted, at measured ^{14}C-radiolabeled DPO dose levels of 0.28 and 1.7 ug/L. Aliquots (2 mL) of exposure water were analyzed for total ^{14}C activity by direct liquid scintillation analysis, with proper correction for quenching. Fish muscle tissue was analyzed for total combustible ^{14}C activity using a Beckman Biological Material Oxidizer. Whole fish tissue was also extracted with diethyl ether of potassium hydroxide digests and analyzed by gas chromatography/mass spectrometry (GC/MS) for DPO and metabolites. Kinetic rate constants were calculated and optimized using a non-linear least squares program. The bioconcentration factor (BCF) was calculated from the values of the uptake (K_1) and clearance (k_2) rate constants, using a simple two-compartment model (BCF = K_1/ k_2).
Result	:	A mean uptake rate constant (K_1) of 5.5 (+/- 0.5) mL/g/hr and a mean clearance rate constant (k_2) of 0.028 (+/- 0.003) hr^{-1} were measured from the two exposure concentrations, yielding an average steady-state BCF value in trout muscle of 196 (+/- 26) for DPO. The measured elimination rate constant produces a pseudo first-order elimination half-life for DPO from rainbow trout tissue of 25 hours. The measured lipid content of the fish used in this study was 1.0-1.5% by weight. These short-term exposure rate constants were confirmed by good agreement of estimated steady-state fish residues with measured ^{14}C residues in fish in the longer-term, 42-day exposure studies. Within the limits of analytical detection, there did not appear to be any metabolites of DPO observed in the extracted whole fish tissue. As a result, the uptake, storage, and clearance of ^{14}C-DPO was considered to be the parent compound. In summary, the relatively low steady-state BCF value of DPO in rainbow trout tissue is explained by the biological half-life of ~25 hours for

elimination of DPO from trout muscle. Concomitant longer-term exposures conducted along side the 96-hr experiments in this study suggest that determination of uptake and clearance rate constants from short-term studies are consistent with rate constants from steady-state conditions in longer-term exposures.

Reliability : (2) valid with restrictions
Study is generally consistent with OECD guidance.

Flag : Supplemental study for SIDS endpoint

18.7.2003 (3)

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	static
Species	:	Oncorhynchus mykiss (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no
LC50	:	= 4.2
Method	:	other
Year	:	1980
GLP	:	yes
Test substance	:	other TS
Method	:	Followed methodology outlined in Methods of Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians, US EPA Ecolog. Res. Series, 1975. Ten fish (average weight of 0.31 g and mean length of 29.2 mm obtained from Beitey Resort, Valley WA, USA), fasted 48 hr before treatment, were tested for up to 96-h at 5 nominal concentrations of DPO in acetone between 1 and 10 mg/L. Test material was not measured during the test. Both a positive control (Antimycin A) and a solvent control were used. Temperature was maintained at 12 deg. C. Photoperiod was 16 hours light and 8 hours dark. Fish were observed for signs of toxicity and mortality at least daily. LC50 values were calculated using a computerized LC50 program developed by Stephen et al, 1978, US EPA Duluth, MI). Tests were conducted in 5 gal glass vessels containing 15 L. lab well water and held at a constant temp. of 12 deg. C.
Result	:	96-h LC50 (CI 95%) = 4.2 (3.2-5.6) mg/L; the 48-Hr LC50 (plus CI) was: 6.0 (4.7-7.8). The dOxy was 60-100%, the pH constant in all groups at 7.8, and all groups had a NH3 level <0.28 ppm (well below the toxic limit). Water quality indices at study start were found to be: dO2 = 9.3 mg/L., pH = 8.2; Hardness (CaCO3) = 225 ppm, alkalinity (CaCO3) = 368 ppm. Total ammonia was < 0.05 in all test groups. No deaths occurred in either control group or in the 1, 1.8 or 3.2 mg DPO /ml/day test groups throughout the study. Deaths occurred at the 5.6 and 10 mg/L concentrations at 24, 48 and 96-h, as follows: 0 %,. 50%, 100%, respectively at 5.6 mg/L and 50%, 90%, and 100%, respectively, at 10 mg/L. Loss of equilibrium and surfacing were observed at the two higher test levels.
Test substance	:	Unspecified but likely commercial grade with purity >99%.
Reliability	:	(2) valid with restrictions Study is consistent with OECD guidance and was conducted under GLPs.
Flag	:	Critical study for SIDS endpoint

25.11.2002 (7)

Type	:	static
Species	:	Pimephales promelas (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no
NOEC	:	= 10
LC50	:	= 13
Method	:	other
Year	:	1980
GLP	:	yes
Test substance	:	other TS
Method	:	Followed design in Methods of Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians, US EPA Ecolog Res Series, 1975. Groups of 10 fathead minnows (mean weight of 0.24 g; mean length of 25.1 mm, obtained from Fattig Fish Hatchery, Brady, NE, USA) were tested for up to 96-h at 5 DPO (in acetone) nominal test concentrations. Test material was not measured during test. Untreated and solvent controls

and a positive control (antimycin A) were also employed. Temperature was maintained at 22 deg. C. Photoperiod was 16 hours light and 8 hours dark. Studies were conducted in 5 gal glass jars filled with 15 L well water. Test concentrations had a hardness (CaCo3) of 225 ppm, alkalinity (CaCO3) of 368 ppm, NH3 < 0.28, pH ranging between 7.6-7.7 and dis. Oxygen ranging between 9.0 and 3.0 mg/L. LC50 values and CI were calculated using the method of Stephen et al, 1978. US EPA Environ. Res. Lab, Duluth, MI, USA.

Remark : Dissolved oxygen values in control group was >40 % saturation throughout study. However, in some DPO-treated groups the oxygen level fell below that level during the last 24 hrs of testing. No impact on mortality was observed in this study as there were no additional deaths observed at any test concentration during this period of the study.

Result : 96-h LC50 (95% CI) = 13 (10-18) mg/L; 48-h LC50 (95%CI) = 13 (10-18) mg/L; 24-h LC50 (95% CI) = 34 (18-56) mg/L. Following was the % mortality seen at each test concentration at 24, 48 and 96h respectively: control- 0,0,0; solvent control -0,0,0; 10 mg/L- 0,0,0; 18 mg/L- 0, 100, 100; 32 mg/L- 40, 100, 100; 56 mg/L- 100, 100, 100; 100 mg/L- 100, 100, 100; loss of equilibrium was noted in fish at test concentrations of 18 mg/L and higher. An oily substance was noted at all test levels.

Reliability : (2) valid with restrictions
Well conducted and documented study with a design similar to OECD 203. Study provided as Supplementary, as the previous acute fish study included in this dossier has been used to fulfill this HPV Endpoint.

25.11.2002 (8)

Type : other
Species :
Exposure period : 96 hour(s)
Unit : mg/l
Analytical monitoring :
LC50 : = 1.079
Method : other
Year : 2002
GLP :
Test substance :
Method : An acute fish 96-h LC50 was calculated using ECOSAR from the US EPA. The SAR for neutral organics was used. The equation used was Log LC50= -0.94 log Kow + 1.75, which has a Coefficient of Determination (R2) = 0.942 for the training set. The structure was determined from the CAS RN, as stored in the accompanying database of SMILES notations within ECOSAR. Calculations used measured values for MP, water solubility, and Kow.
Test substance : Diphenyl oxide
Reliability : (2) valid with restrictions
Supplemental information using estimation model recommended by US EPA. As this material is an ether, it is expected to be highly stable in water; thus, the value calculated should be representative of the test material modeled.

26.11.2002 (15)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type : static
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
Analytical monitoring : no
NOEC : = 1
EC50 : = 1.7

EC100	:	= 10
Method	:	other
Year	:	1980
GLP	:	yes
Test substance	:	other TS
Method	:	Study design followed recommendations from the US EPA Committtee on Methods for Toxicity Testing with Fish, Macroinvertebrates and Amphibians, Ecolog. Res. Series, 1975. Groups of 10 first instar D. magna (inhouse colony) were exposed to one of 5 nominal test concentrations of DPO in acetone ranging in logarithmic series from 1 to 10 mg/l (i.e. 10, 5.6, 3.2, 1.8 and 1 mg/l); both a solvent control and an untreated control were also used. All concentrations were run in duplicate. Test material was not measured during test. Each group was placed in a 250 ml glass beaker filled with 200 ml well water, held at 20 degrees C. with 16 hrs artificial light per day @ 50-70 footcandles. Test article was suspended in 1 ml acetone and added to the respective beaker. Daphnia were observed every 24 hrs for morbidity and mortality. Water quality indices (temp., pH, dissolved oxygen) were measured prior to study start and at the end of the study. Water hardness (CaCO3) was 225 ppm. LC50 values (24 and 48 hr) were calculated using the method of Stephen, Busch, Smith, Burke and Anderson, USEPA Duluth Labs computer model, 1978. pH ranged between 8.0-7.8 and dis. Oxygen betwen 9.5-9.4 in all groups.
Result	:	The 48-h LC50 (CI 95%) = 1.7 (1.5-1.9) mg/L. The 24-h LC50 (95% CI) = 2.2 (1.9-2.5) mg/L. The NOEC (48-h) = 10 mg/L. Following are the levels (%) mortality seen in each test concentration at 24-h and 48-h, respectively: control- 0, 0; solvent control - 0, 0; 1 mg/L - 0, 0; 1.8 mg/L - 0, 70; 3.2 mg/L - 35, 95; 5.6 mg/L- 85, 100; 10 mg/L - 100, 100.
Test substance	:	DPO unspecified but likely commercial grade with purity of > 99%.
Reliability	:	(2) valid with restrictions Study design consistant with OECD 202.
Flag	:	Critical study for SIDS endpoint

25.11.2002 (6)

Type	:	other
Species	:	
Exposure period	:	48 hour(s)
Unit	:	mg/l
Analytical monitoring	:	
EC50	:	= 1.346
Method	:	other
Year	:	2002
GLP	:	
Test substance	:	other TS
Method	:	An acute Daphnia 48-h LC50 was calculated using ECOSAR, from the US EPA. The SAR for neutral organics was used. The equation used was Log LC50 = 1.72-0.91 log Kow, which has a Coefficient of Determination (R2) = 0.992 for the training set. The structure was determined from the CAS RN, as stored in the accompanying database of SMILES notations within ECOSAR. Calculations were made using measured values for MP, water solubility, and Kow.
Test substance	:	Diphenyl oxide
Reliability	:	(2) valid with restrictions. Supplemental information provided using estimation model recommended by US EPA. As this material is an ether, it is expected to be highly stable in water; thus, the values calculated should be representative of the test material modeled.

26.11.2002 (15)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species	:	Selenastrum capricornutum (Algae)
Endpoint	:	growth rate
Exposure period	:	96 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no
EC50	:	= 2.5
Method	:	other
Year	:	1980
GLP	:	yes
Test substance	:	other TS
Method	:	Study procedures followed guidance found in The S. capricornutum Printz Algal Assay Test. Experimental Designs, Application and Data Interpretation. Corvallis, Environmental Research Laboratory, US EPA, 1978. Study designed to measure both decrease of in vivo chlorophyll a and a decrease in cell number over time. Algae was obtained from the US EPA Env. Res. Lab, , Corvallis, OR, USA. A least 2 x 10E4 cells/mL were incubated at 24 deg C with 4000 lux illumination at 5 nominal test concentrations (0.6, 1.2, 2.5, 5, and 10 mg/L). Both an untreated control and a solvent (triethylene glycol) control group were also included in the test. All test concentrations were conducted in triplicate. Test material was not measured during the test. The test system was 125 ml flasks containing 50 ml test medium, the pH ranged between 7.2-7.6 throughout the study. Photoperiod was 24 hours light. Chlorophyll measurements were taken using a fluorometer; cells counts were made using a hemacytometer and compound microscope. Data were treated statistically by using the probit method of Finney (1971) followed by linear regression analysis. A probablitity factor of 5% was used.
Result	:	Based on the decrease in chlorophyll the following EC50 values (95%CI) were calculated: 96-h = 2.5 (1.2-5.4) mg/L; at 72-h and 48h = >2.5<5.0 mg/L; at 24-h = > 10 mg/L. Based on the number of decreased cells, the 96-h LC50 (95% CL) = 2.5 (1.2-5.3) mg/L
Test substance	:	DPO unspecified but likely commercial grade with purity of > 99%.
Reliability	:	(2) valid with restrictions GLP conducted study following a regulatory-recommended study design.
Flag	:	Critical study for SIDS endpoint

25.11.2002 (10)

Species	:	other algae
Endpoint	:	
Exposure period	:	96 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no
EC50	:	= .955
Method	:	other
Year	:	2002
GLP	:	
Test substance	:	other TS
Method	:	An acute green algal 96-h LC50 was calculated using ECOSAR, from the US EPA. The SAR for neutral organics was used. The equation used was Log 96-h EC50 = 1.466-0.885 log Kow, which has a Coefficient of Determination (R2) = 0.91 for the training set. The structure was determined from the CAS RN, as stored in the accompanying database of SMILES notations within ECOSAR. Calculations were made using measured values for MP, water solubility and Kow.
Test substance	:	Diphenyl oxide.
Reliability	:	(2) valid with restrictions Supplemental information using US EPA recommended estimation model. As this material is an ether, it is expected to be highly stable in water. The value calculated should be representative of the test material modeled.

26.11.2002 (15)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

4.6.1 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO OTHER NON-MAMM. TERRESTRIAL SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	male/female
Number of animals	:	20
Vehicle	:	other: undiluted
Value	:	= 2450 mg/kg bw
Method	:	other
Year	:	1977
GLP	:	no
Test substance	:	other TS
Method	:	DPO was administered undiluted via single dose gavage to groups of 5 fasted Sprague-Dawley rats (either 2 or 3 males per group; concomitantly, 3 or 2 females per group) per dose group at dosages of 2000, 2510, and 3160 mg/kg. Rats were observed approximately 1 hour after dosing and twice daily over a 14-day observation period for signs of toxicity. Body weights were recorded individually at inception and on test days 7 and 14. All rats found dead or sacrificed by design at the end of the observation period were given a gross necropsy. LD50, CL and slope calculated by the method of deBeer,E. 1945. J. Pharmacol. Experimen. Ther. 85:1. Humidity, temperature and lighting were controlled. Food was administered ad libitum.
Result	:	No deaths (0/5) at 2000 mg/kg; 3/5 dead at 2510 mg/kg and 5/5 dead at 3160 mg/kg. Generalized weakness observed prior to death; necropsy of decedents resulted in identification of liver and lung hyperemia and acute gastrointestinal inflammation. 95% Confidence Limits

of 2200-2720 mg/kg

Test substance	:	DPO of >99% purity
Reliability	:	(2) valid with restrictions Study conducted prior to, but consistent with, pending US GLPs 21 CFR 58, and effective 20 June, 1979. The study design used is consistent with guidelines and endpoints listed in OECD Test Guideline 401, although fewer animals were used. Results in this study are consistent with a similar degree of oral toxicity reported in the literature (Weir, 1974. Fd Cosmet Tox 12:707).
Flag	:	Critical study for SIDS endpoint

25.11.2002 (14)

5.1.2 ACUTE INHALATION TOXICITY

5.1.3 ACUTE DERMAL TOXICITY

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

5.2.2 EYE IRRITATION

5.3 SENSITIZATION

5.4 REPEATED DOSE TOXICITY

Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	oral feed
Exposure period	:	90- days
Frequency of treatment	:	Daily
Post obs. period	:	4-weeks
Doses	:	0, 200, 1000, 5000 ppm
Control group	:	yes, concurrent no treatment
NOAEL	:	> 5000 ppm
Method	:	OECD Guide-line 408 "Subchronic Oral Toxicity - Rodent: 90-day Study"
Year	:	1990
GLP	:	yes
Test substance	:	other TS
Method	:	Four groups of Sprague Dawley albino rats (10/sex) were exposed to graded concentrations of 0, 200, 1,000, or 5,000 ppm DPO in the diet for 13 weeks. An additional 10 rats/sex/group were designated as recovery rats and were retained for 4 weeks after the 13-week feeding period and received untreated rodent chow during that latter interval. Test article was prepared neat in a premix and subsequent diets prepared weekly. Analyses were conducted periodically for homogeneity and test article concentration levels. Daily physical exams and clinical observations were performed on each animal. Body weights and food consumption were recorded weekly for each animal. Ophthalmoscopic exams were performed

at study start and after 13 weeks on test for all animals. The following clinical exams were performed on each animal prior to necropsy: GLU, CK, ALT, SGPT, AST, SGOT. ALKP, GGT, BUN, CREA, Na, K, Ca, Cl, Phos, TPRO, ALB, TBIL, CHOL,RBC, HGB, MCV, WBC, PLAT, GLOB, A:G ratio, HCT, MHC, MCHC, urine appearance, volume, Spec. grav., occult blood, protein, pH, ketones, urobilinogen, GLU, BILI, sediments. Complete necropsies were performed on all rats at study termination and a set of 46 tissues collected for microscopic exam. Histopathologic examinations were performed on all animals from the control and HD groups after 13 weeks, as well as lungs, liver, kidneys, and gross lesions from 200 ppm and 1000 ppm animals after 13 weeks. Absolute and relative organ (brain, gonads, heart, kidneys, liver and spleen) weights were recorded at necropsy. Body weights and gains and food consumption and ratio data were evaluated using multivariate repeated-measure analysis of variance while other data were log-transformed and statistically analyzed using both multivariate and univariate two-factor fixed-effect analysis of variance (ANOVA). All comparisons for combined data of sexes were conducted using the Dunnett's test for multiple comparisons. A minimum significance level of $p<0.05$ was used throughout. Gonads of all high dose and control animals were examined microscopically

Remark : Systemic NOEL considered 5000 ppm as findings at 1000/5000 ppm considered palatability induced

Result : Periodic analyses of feed confirmed homogeneity and test article concentration. Dosage determinations: males - 0, 11.7, 60.7 & 301.1 mg/kg/day; females - 0,14.5, 73.9, & 334.8 mg/kg/day. None of the test or recovery animals died during the 13-week feeding or 4-week treatment/recovery periods. No signs of test article-related clinical toxicity were observed during the 13-week treatment period, nor were any adverse signs noted during the recovery period. Mean weekly body weight and food consumption were significantly decreased in 5000 ppm males and females during entire 13-week treatment period. Statistically significant decreases in mean body weight and food consumption also were noted in the 1000 ppm female group during most of the study. These changes were attributable to decreased palatability of test diet, as evidenced by statistically significant increases in food consumption and/or body weight gain and increased food conversion ratios during one or more weeks of recovery. No treatment-related clinical chemistry, urinalysis, or hematology were observed, nor were there ocular manifestations of toxicity. The few statistically significant differences noted in the above parameters were either not dose-related, within range of in-house historical values or occurred only in recovery animals. No absolute organ weight changes attributable to treatment were observed, nor were there any gross lesions or histopathological effects related to treatment, including male and female gonads. The few statistically significant differences in relative weights observed in both sexes in the high dose group and mid dose females were attributed to their substantive decreased body weights seen at termination of treatment and not direct target organ toxicity. No treatment-related gross lesions were observed in this study. No histopathological effects related to DPO-treatment were observed, including male and female gonads.

Test substance : Commercial grade DPO with presumed purity > 98%.

Reliability : (1) valid without restriction
Study conducted under GLPs and consistent with OECD Test Guideline 408.

Flag : Critical study for SIDS endpoint

25.11.2002 (5)

5.5 GENETIC TOXICITY 'IN VITRO'

Type : Ames test

System of testing : Spot test and Plate Incorporation Assay

Concentration	:	ST-10 mg/plate; PIA-0.1, 1, 10, 33, 100 and 500 ug/plate
Cycotoxic conc.	:	1 mg/plate w & w/o activation in Spot test; lower levels in PIA
Metabolic activation	:	with and without
Result	:	negative
Method	:	other
Year	:	1978
GLP	:	no
Test substance	:	other TS
Method	:	Methodology employed prior to codification of, but consistent with OECD guideline 471. Media and handling procedures and preparation of liver microsomal fractions (S-9) followed the procedure outlined in Ames et al. Mut. Res. 31:347-364. Salmonella tester strains used were TA1535, TA1537, TA98, and TA100. DMSO was used as a solvent. Toxicity test using TA100 conducted at 0.1, 1, 3 and 10 mg/plate with and without activation. A toxic response was considered a concentration which eliminated background lawn or reduced it to individual colonies. Plate Incorporation assay run in triplicate. A Spot Test was conducted using all four Salmonella tester strains prior to conduct of the plate incorporation assay, where it was applied directly to the center of the plate on sterile paper discs. DPO was evaluated at a maximum level of 10 mg/plate, with and without mouse and rat microsomal preparations. After 48 hours incubation, the number of colonies on the plate and pattern of colonies were visually examined. A positive response was judged by formation of a halo of revertant colonies around the plate center. A Plate Incorporation Assay was performed using 6 concentrations of DPO in DMSO resulting in levels of 0.1, 1, 10, 33, 100 and 500 ug DPO/plate. Tests were performed by adding bacterial suspensions, test sample and metabolic activation (S-9) mix (if appropriate) to histidine-biotin top agar, rapidly mixed and poured onto minimal glucose plates. Colonies were counted after 48-hours incubation. Each concentration was run in triplicate. Tester strains TA1535, TA 1537, TA 98, and TA 100 each with and without metabolic activation, were assayed at each DPO concentration. The highest concentration tested corresponded to one-half the lowest concentration giving severe toxicity in the Toxicity Test. Appropriate solvent and negative controls were run. Following were used as positive controls: TA1535 - $NaNO_2$ and Tris (2,3-dibromopropyl) phosphate for -/+ S-9, respectively; TA1537 - 9-aminoacridine and 2-aminoanthracene for -/+ S-9, respectively; TA98 - 4-nitroquinoline-N-oxide and 2-acetamidofluorene for -/+ S-9, respectively; and TA100 - 4-nitroquinoline-N-oxide and benzo(a)pyrene for -/+ S-9, respectively. S9 co-factor was prepared according to Mut. Res. 31:347-64. Revertants/plate were transformed to log 10 and within pooled variance for calculation; comparisons were made via t-test ($p<0.01$).
Result	:	Levels of 1 mg/plate w/wo activation produced severe toxicity; No mutagenic activity at max. conc. used of 10 mg/plate in all 4 tester strains in the Spot Test; In the Plate Incorporation Assay, toxicity was observed in strains TA98 and TA100 at 500 ug/plate and 33 ug/plate and higher for TA1535 and TA1537. No mutagenic activity was detected towards any of the 4 tester strains, with or without metabolic activiation.
Test substance	:	Purity of test sample was > 99%
Reliability	:	(2) valid with restrictions Study conducted prior to , but consistent with pending US GLP 21 CFR 58, effective 20, June 1979. Results are consistent with those reported from NTP program and summarized in Haworth et al.1983. Environ. Mutagen. 5:3-142
Flag	:	Critical study for SIDS endpoint

25.11.2002 (12)

Type	:	Chromosomal aberration test
System of testing	:	CHO Cells
Concentration	:	10,50,100 &150 ug/ml (no S-9); 5,30,50 ug/ml (with S-9)
Cycotoxic conc.	:	150 ug/ml (with S-9)
Metabolic activation	:	with and without

Result	:	negative
Method	:	OECD Guide-line 473 "Genetic Toxicology: In vitro Mammalian Cytogenetic Test"
Year	:	1978
GLP	:	yes
Test substance	:	other TS
Method	:	Preliminary cytotoxicity study used 5,50,100,125,500,750,1000,2500,5000 ug/ml with and without metabolic activation. In this study, cells were exposed to the test article for 5 hours, washed, and incubated in fresh BrdU-containing medium for an additional 27 hours. To arrest cells in metaphase, the flasks contained Colcemid for the last 2-3 hours of incubation. Cells were then harvested, and Giesma-stained chromosome preparations were prepared and examined. Cell kinetics were based on the number of cell cycles completed after exposure to DPO using 100 metaphase cells for the evaluation. In the definitive study, DPO was incubated in CHO cell cultures, both with and without metabolic activation. Each evaluation was performed with cells from duplicate flasks. Based on the preliminary study results of proliferation kinetics and cytotoxic effects, DPO was evaluated with and without metabolic activation at optimized concentrations with 5 hour exposure followed by washing and then 18 hrs of additional incubation; After cell harvest, Giesma-stained chromosomal preparations were prepared on slides and at least 50 cells/flask (100 cells/dosage) were evaluated. All slides were scored blind and statistically analyzed using a "t"-test to compare pairwise each treatment group with the control group using aberrants per cell. The proportion of aberrant metaphases were analyzed using Chi-square analysis. Significance was generally determined at the $p<0.05$ probability level. Dosing solutions prepared in acetone. N-nitrosodimethylamine and MNNG, used as positive controls.
Result	:	Preliminary Study - Cytotoxicity seen at dosages above 500 ug/ml without S-9 and above 250 ug/ml with S-9; cell proliferation times increased at and above 250 ug/ml without S-9 and at and above 50 ug/ml with S-9; Definitive Study - DPO concentrations of 10, 50, 100 and 150 ug/ml (without S-9) and 5, 30 and 50 ug/ml (with S-9) were used. The 150 ug/ml concentration was cytotoxic. DPO did not produce significant increases in the percentage of structural aberrations per cell at any treatment concentration. Both positive control materials elicited the expected increases in aberrations, confirming the sensitivity of the assay to known clastogens.
Test substance	:	DPO with purity > 99%
Reliability	:	(1) valid without restriction GLP study which meets OECD Guideline 473 parameters.
Flag	:	Critical study for SIDS endpoint

25.11.2002 (13)

5.6 GENETIC TOXICITY 'IN VITRO'

5.7 CARCINOGENITY

5.8 TOXICITY TO REPRODUCTION

5.9 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species	:	rat
Sex	:	female
Strain	:	Sprague-Dawley

Route of admin.	:	gavage
Exposure period	:	Gestation days 6-15
Frequency of treatment	:	Daily 1X
Duration of test	:	Through gestation day 15
Doses	:	50, 200, 500 mg/kg/day
Control group	:	yes, concurrent vehicle
NOAEL Maternalt.	:	>= 50 mg/kg bw
NOAEL Teratogen	:	>= 500 mg/kg bw
NOAEL Embryotoxicity	:	>= 500 mg/kg bw
NOAEL Fetotoxicity	:	>= 500 - mg/kg bw
Method	:	OECD Guide-line 414 "Teratogenicity"
Year	:	1986
GLP	:	yes
Test substance	:	other TS
Method	:	DPO was mixed with corn oil and administered to groups comprised of 24 mated Charles River CD female rats each at dosage levels of 0, 50, 200 or 500 mg/kg/d. Single oral daily dosages were administered at a volume of 5 ml/kg by gavage, on gestation days 6-15. Approximately 1/2 of the fetuses in each litter were processed for soft-tissue evaluations while the other half for skeletal evaluations. Statistical evaluation of equality of means was made by the appropriate one-way analysis of variance technique (ANOVA) for parametric procedures and Kruskal-Wallis test for nonparametric procedures were used after applying Bartlett's test for determination of equal variance. Statistical tests for trend, using either standard regression techniques (parametric cases) or Jonckheere's test in nonparametric cases. Levels of statistical significance used were either $p<0.05$ or $p<0.01$.
Result	:	2 deaths occurred at 500 mg/kg. Statistically reduced maternal weight gain and food consumption were observed at 200 and 500 mg/kg/d. Excessive alopecia, salivation and/or anogenital staining was observed but no pattern of treatment relationship could be determined. No effects observed on fetal resorptions, fetal viability, postimplantation loss or total implantations. Mean litter weights in treated and control groups were similar. No significant increases were observed in incidence of malformations or variations at any treatment level.
Test substance	:	73.5% DPO & 26.5% biphenyl mixed in corn oil at volume of 5 ml/kg
Reliability	:	(1) valid without restriction GLP-conducted study which meets OECD Test Guideline 414. Lack of any developmental toxicity observed in this study obviates any concern of differentiating findings between either of the major components in this test mixture.
Flag	:	Critical study for SIDS endpoint

25.11.2002 (9)

5.10 OTHER RELEVANT INFORMATION

5.11 EXPERIENCE WITH HUMAN EXPOSURE

(1) AOP, v. 1.8. 1997. Syracuse Research Corp., Syracuse, NY.

(2) Banerjee, S, Yalkowski, SH and SC Valvani. 1980. Environ Sci Technol 14:1227 (measured value)

(3) Dow Chemical study No. WC-73015 (1973). Bioconcentration of diphenyl oxide in trout.

(4) Dow Chemical study No. ES-106 (1976). Biodegradation of diphenyl oxide.

(5) IITRI Project No. L8100 (Study no. 1482) Thirteen-Week Oral (diet) Toxicity Study of Diphenyl Ether in Rats; also published in The Toxicologist 12 (1):117 (1992).

(6) Solutia study no. AB-80-242. Acute Toxicity of DPO (Diphenyl Oxide) to Daphnia magna.

(7) Solutia study no. AB-80-243. Acute Toxicity of DPO to Rainbow Trout.

(8) Solutia study no. AB-80-244. Acute Toxicity of Diphenyl Oxide to Fathead Minnows.

(9) Solutia study no. BD-86-379. A Developmental Toxicity Study in Rats with THERMINOL® VP-1 Heat Transfer Fluid.

(10) Solutia study no. BN-80-241. Toxicity of DPO (Diphenyl oxide) to the freshwater alga S. capricornutum.

(11) Solutia study no. ES-83-SS-23. Biodegradaton screening of biphenyl, diphenyl oxide, and THERMINOL® VP-1 Heat Transfer Fluid.

(12) Solutia Study No. LF-78-168. Salmonella Mutagenicity Assay of Diphenyl Oxide.

(13) Solutia Study No. PK-86-423; In Vitro Chromosome Aberration Analysis in Chinese Hamster Ovary (CHO) Cells. EPA OTS Doc. 86-890000343.

(14) Solutia Study No. YO-77-72. Toxicity Studies on Diphenyl oxide. EPA TSCATS no. 86-8900000346

(15) US EPA ECOSAR model, v. 0.99f.

(16) Vershueren (ed.). 1983. Handbook on Environmental Data of Organic Compounds. 2nd edit. Van Nostrand Reinhold Co, NY.

7.1 END POINT SUMMARY

7.2 HAZARD SUMMARY

7.3 RISK ASSESSMENT